

CLAIMS

What is claimed is:

1. A method of measuring the level of lipid peroxidation in a mammal suspected of having an oxidant stress syndrome or disease, said method comprising

a) obtaining a first sample of a tissue or body fluid from said mammal;

b) assessing the level of an isoprostane molecular marker for lipid peroxidation present in said first sample; and

c) comparing the level of said isoprostane molecular marker present in said first sample with the level of said isoprostane molecular marker present in a second sample of a tissue or body fluid obtained from an otherwise identical mammal which is not afflicted with an oxidant stress syndrome or disease, wherein an elevated level of said isoprostane molecular marker in said first sample relative to the level of said isoprostane molecular marker in said second sample, is indicative of an elevated level of lipid peroxidation in said mammal, thereby indicating the presence of an oxidant stress syndrome or disease in said mammal.

2. The method of claim 1, further comprising after a) and prior to b) isolating from said first sample said isoprostane molecular marker.

3. The method of claim 1, wherein said elevated level of lipid peroxidation comprises an elevated level of a reactive oxygen species (ROS).

4. The method of claim 1, wherein said elevated level of lipid peroxidation comprises an elevated level of inflammation.

5. The method of claim 4, wherein said elevated level of inflammation comprises elevated cyclooxygenase (COX) activity.

6. The method of claim 1, wherein said oxidant stress disease is Alzheimer's disease.

7. The method of claim 1, wherein said isoprostane molecular marker is selected from the group consisting of $iPF_{2\alpha}$ -III, $iPF_{2\alpha}$ -VI and 8,12-*iso*- $iPF_{2\alpha}$ -VI.

8. The method of claim 1, wherein said tissue is brain tissue.

9. The method of claim 8, wherein said brain tissue is selected from the group consisting of brain frontal pole tissue and brain temporal pole tissue.

10. The method of claim 1, wherein said body fluid is selected from the group consisting of cerebrospinal fluid (CSF), plasma and urine.

11. A method of diagnosing an oxidant stress syndrome or disease in a mammal, said method comprising

- Sub A2
- a) obtaining a first sample of a tissue or body fluid from said mammal;
 - b) assessing the level of said isoprostane molecular marker present in said first sample; and
 - c) comparing the level of said isoprostane molecular marker present in said first sample with the level of said isoprostane molecular marker present in a second sample of a tissue or body fluid obtained from an otherwise identical mammal which is not afflicted with said oxidant stress syndrome or disease, wherein an elevated level of said isoprostane molecular marker in said first sample relative to the level of said isoprostane molecular marker in said second sample, is indicative of an elevated level of lipid peroxidation in said mammal, whereby said oxidant stress syndrome or disease is diagnosed in said mammal.

12. The method of claim 11, further comprising, after a) and before b) isolating from said first sample said isoprostane molecular marker.

Sub A3

13. A method of measuring the level of an isoprostane molecular marker for lipid peroxidation in a mammal suspected of having an oxidant stress syndrome or disease, said method comprising

- a) obtaining a sample of a tissue or body fluid from said mammal;

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- b) isolating from said sample said isoprostane molecular marker by using a total lipids solvent extraction method;
 - c) assaying said isoprostane molecular marker from b); and
 - d) quantifying the level of said isoprostane molecular marker.

14. The method of claim 13, wherein said assaying comprises using a gas chromatography/mass spectrometry assay method which comprises a synthetic homologous isoprostane standard, and further wherein said quantifying is performed using peak area or peak height ratios.

15. The method of claim 13, wherein said oxidant stress disease is Alzheimer's disease.

16. The method of claim 13, wherein said isoprostane molecular marker is selected from the group consisting of $iPF_{2\alpha}$ -III, $iPF_{2\alpha}$ -VI and 8,12-*iso*- $iPF_{2\alpha}$ -VI.

17. The method of claim 13, wherein said tissue is brain tissue.

18. The method of claim 17, wherein said brain tissue is selected from the group consisting of brain frontal pole tissue and brain temporal pole tissue.

19. The method of claim 13, wherein said body fluid is selected from the group consisting of cerebrospinal fluid (CSF), plasma and urine.

20. A method of identifying a compound useful for the treatment of Alzheimer's disease in a mammal, said method comprising

- a) measuring the level of an isoprostane molecular marker for lipid peroxidation in either a sample of a tissue or body fluid obtained from a first mammal prior to administering said compound, or, in a sample of a tissue or body fluid obtained from an otherwise identical second mammal which is not to be administered said compound;
- b) administering said compound to said first mammal;

c) thereafter measuring the level of said isoprostane molecular marker in a tissue or body fluid obtained from said first mammal; and

d) comparing the level of said isoprostane molecular marker measured in c) with the level of said isoprostane molecular marker measured in a), wherein when the level of said isoprostane molecular marker measured in c) is reduced relative to the level of said isoprostane molecular marker measured in a), a compound useful for the treatment of Alzheimer's disease in a mammal is identified.

21. The method of claim 20, wherein said isoprostane molecular marker of lipid peroxidation is selected from the group consisting of $iPF_{2\alpha}$ -III, $iPF_{2\alpha}$ -VI and 8,12-*iso*- $iPF_{2\alpha}$ -VI.

22. The method of claim 20, wherein said tissue is brain tissue selected from the group consisting of brain frontal pole tissue and brain temporal pole tissue.

23. The method of claim 20, wherein said body fluid is selected from the group consisting of cerebrospinal fluid (CSF), plasma and urine.

24. A method of identifying an effective amount of a compound useful for the treatment of Alzheimer's disease in a mammal, said method comprising

a) measuring the level of an isoprostane molecular marker for lipid peroxidation in either a sample of a tissue or body fluid obtained from a first mammal prior to administering said compound, or, in a sample of a tissue or body fluid obtained from an otherwise identical second mammal which is not to be administered said compound;

b) administering to said first mammal an amount of said compound;

c) thereafter measuring the level of said isoprostane molecular marker in a tissue or body fluid obtained from said first mammal; and

d) comparing the level of said isoprostane molecular marker measured in c) with the level of said isoprostane molecular marker measured in a), wherein when the level of said isoprostane molecular marker measured in c) is reduced relative to the level of said isoprostane molecular marker measured in a), an effective amount of a compound useful for the treatment of Alzheimer's disease in a mammal is identified.

25. A method of determining the optimal concentration of a compound useful for the treatment of Alzheimer's disease, said method comprising monitoring the level of an isoprostane molecular marker for lipid peroxidation in a series of mammals administered said compound at a series of concentrations of compound, wherein the concentration of said compound which results in maximal reduction of the level of said isoprostane molecular marker in one or more of said series of mammals, which concentration is not toxic to said mammals, is said optimal concentration.

26. A method of determining the optimal dosage frequency of a compound useful for the treatment of Alzheimer's disease, said method comprising monitoring the level of an isoprostane molecular marker for lipid peroxidation in a series of mammals administered said compound at a series of dosage frequencies, wherein the dosage frequency of said compound which results in maximal reduction of the level of said isoprostane molecular marker in one or more of said series of mammals, which dosage is not toxic to said mammals, is said optimal dosage frequency.

27. The method of claim 25, wherein said compound is an antioxidant compound.

28. The method of claim 25, wherein said compound is an anti-inflammatory compound, wherein said compound is administered at a series of concentrations effective to inhibit the activity of a cyclooxygenase (COX) enzyme in a mammal.

29. A method of identifying a compound useful for reducing the level of an isoprostane molecular marker for lipid peroxidation in a sample of a tissue or body fluid obtained from a first mammal, said method comprising

a) measuring the level of said isoprostane molecular marker in either a sample of a tissue or body fluid obtained from said first mammal prior to administering said

compound, or, in a sample of a tissue or body fluid obtained from an otherwise identical second mammal which is not to be administered said compound;

b) administering said compound to said first mammal;

c) thereafter measuring the level of said isoprostane molecular marker in a tissue or body fluid sample obtained from said first mammal;

d) comparing the level of said isoprostane molecular marker measured in c) with the level of said isoprostane molecular marker measured in a), wherein when the level of said isoprostane molecular marker measured in c) is reduced relative to the level of said isoprostane molecular marker measured in a), a compound useful for reducing the level of an isoprostane molecular marker in a mammal is identified.

30. The method of claim 29, wherein said compound is present in an amount effective to inhibit the activity of a cyclooxygenase enzyme in the brain tissue of said mammal.

31. The method of claim 29, wherein said compound is present in an amount effective to reduce the level of a reactive oxygen species in the brain tissue of said mammal.

32. The method of claim 29, wherein said isoprostane molecular marker of lipid peroxidation is selected from the group consisting of $iPF_{2\alpha}$ -III, $iPF_{2\alpha}$ -VI and 8,12-*iso*- $iPF_{2\alpha}$ -VI.

33. A kit for diagnosing Alzheimer's disease in a mammal, said kit comprising

a) a sample container for carrying a tissue or body fluid sample from said mammal;

b) a solution for use in extraction of an isoprostane molecular marker for lipid peroxidation from said tissue or body fluid sample obtained from said mammal;

c) a negative control solution of said isoprostane molecular marker of lipid peroxidation present at a concentration of about the concentration of said isoprostane

molecular marker present in a tissue or body fluid sample of a mammal which is not afflicted with Alzheimer's disease;

d) a positive control solution of said isoprostane molecular marker of lipid peroxidation present at a concentration of about the concentration of said isoprostane molecular marker in a tissue or body fluid sample of a mammal which is afflicted with Alzheimer's disease;

e) an antibody directed against an isoprostane molecular marker for lipid peroxidation; and

f) an instructional material.

34. A kit for measuring the level of an isoprostane molecular marker for lipid peroxidation in a tissue or body fluid sample obtained from a mammal, said kit comprising

a) a sample container for carrying a tissue or body fluid sample from said mammal;

b) a solution for use in extraction of an isoprostane molecular marker of lipid peroxidation from said tissue or body fluid sample obtained from said mammal;

c) a negative control solution of said isoprostane molecular marker of lipid peroxidation present at a concentration of about the concentration of said isoprostane molecular marker present in a tissue or body fluid sample of a mammal which is not afflicted with Alzheimer's disease;

d) a positive control solution of said isoprostane molecular marker of lipid peroxidation present at a concentration of about the concentration of said isoprostane molecular marker in a tissue or body fluid sample of a mammal which is afflicted with Alzheimer's disease;

e) an antibody directed against an isoprostane molecular marker for lipid peroxidation; and

f) an instructional material.

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